Simple non-invasive fibrosis scores identify patients with NAFLD who progress to advanced fibrosis/cirrhosis: evidence from a large cohort of patients with sequential liver biopsies.

Stuart McPherson, Raluca Pais, Luca Valenti, Joern Schattenberg, Jean-Francois Dufour, Emmanuel Tsochatzis, Sven Franque, Tim Hardy, Marie Boyle, Dina Tiniakos, Vlad Ratziu & Quentin M. Anstee, On behalf of the EPoS Consortium & the European NAFLD Registry

Introduction

Non-alcoholic fatty liver disease (NAFLD) is the most frequent liver disease in many counties. Overall, 30-40% of patients with NAFLD develop progressive liver fibrosis, which can result in cirrhosis. Identifying patients who progress to advanced fibrosis/cirrhosis is important so they can be screened for liver-related complications. Cross sectional studies show that the NAFLD fibrosis score (NFS) and FIB-4 score can accurately rule out advanced fibrosis. It remains unknown whether longitudinal assessment of the NFS and FIB-4 scores can identify patients who progress to advanced fibrosis. Our aim was to assess the utility of the FIB-4 score and NFS at baseline and follow up to predict fibrosis progression from F0-2 to F3-4 and to identify F3-4.

Methods:

NAFLD patients with 2 sequential liver biopsies were identified from 7 European specialist centres. Clinical and laboratory data were collected from the time of liver biopsy. Histological scoring was performed according to the Kleiner criteria. The FIB-4 score and NFS were calculated from blood tests taken at the time of liver biopsy.

Results

From a total of 321 NAFLD patients who had sequential biopsies conducted >1 year apart, 278 patients had stage 0-2 fibrosis at the index biopsy and 50 (18%) of them progressed to advanced fibrosis/cirrhosis (41 F3 and 9 F4) over median follow up time of 4.1 years (IQR 2.1-7.76). The proportion of patients progressing to F3-4 was 5%, 21% and 35% for patients with F0, F1 and F2 at baseline respectively. After multivariate analysis, the FIB-4 score (OR 2.01, 95% CI 1.28-3.4; p=0.003) was the only baseline factor that predicted progression from F0-2 to F3-4. The baseline FIB-4 score predicted progression to F3-4 with modest accuracy (AUROC 0.74, 95% CI 0.65-0.82; p<0.001; optimum cut-off 1.15, 71% sensitive and 69% specific; PPV 30% and NPV 93%). Both the FIB-4 score and the NFS identified patients who developed F3-4 at the follow up biopsy with reasonable accuracy (AUROC for FIB-4 0.76, 71% sensitivity and 67% specificity at cut-off 1.3; AUROC for NFS 0.80, 83% sensitivity and 60% specificity at the cut off -1.455). Both the NFS and FIB-4 score were accurate in identifying patients who progressed to cirrhosis at the second biopsy (AUROC for NFS = 0.85; AUROC for FIB4 0.85)

Conclusions

Longitudinal assessment of the NFS and FIB-4 score can identify patients who progress to advanced fibrosis/cirrhosis with reasonable accuracy. A low FIB-4 score (<1.15) in patients NAFLD can reliably exclude progression to advanced fibrosis over medium-term follow-up periods.